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ORIGINAL ARTICLE

Implications of Early Versus Late Bilateral Pulmonary Infiltrates in Patients with Aneurysmal Subarachnoid Hemorrhage

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Abstract
Introduction Bilateral pulmonary infiltrates occur frequently following aneurysmal subarachnoid hemorrhage (SAH), and may be associated with worse outcomes. The etiology, natural history, and prognosis of infiltrates occurring soon after SAH may differ from the characteristics of infiltrates developing at a later time.
Methods We performed a retrospective cohort study involving 245 consecutive patients with a ruptured cerebral aneurysm to assess the association between "early" ($\leq$72 h) or "late" ($>$72 h) bilateral pulmonary infiltrates and subsequent death or neurologic impairment. We used logistic regression models to adjust for baseline differences in age, level of consciousness, amount of blood on computed tomography, and the presence or absence of clinical vasospasm.
Results Sixty-seven patients (27%) developed bilateral pulmonary infiltrates. Of these, 36 (54%) had early infiltrates, 24 (36%) had late infiltrates, and 7 (10%) had both. Twenty-eight patients (11% of entire cohort) met criteria for acute respiratory distress syndrome (ARDS). Patients with early infiltrates were more likely to have presented with stupor or coma than patients who developed infiltrates later (64% vs. 29%, $P < 0.01$). In multivariable analysis, late pulmonary infiltrates were strongly predictive of poor outcome (OR 5.0, 95% CI 1.9–13.6, $P < 0.01$), while early infiltrates were not (OR 1.2, 95% CI 0.5–3.0, $P = 0.66$).
Conclusions Bilateral pulmonary infiltrates after SAH most often occur within three days of aneurysm rupture. However, only infiltrates occurring beyond this time are independently associated with poor outcome. Increased emphasis on the prevention of late pulmonary complications has the potential to improve outcomes in SAH.

Keywords Pulmonary infiltrates · Pulmonary edema · Acute lung injury · Acute respiratory distress syndrome · Neurogenic pulmonary edema · Neurogenic stress cardiomyopathy · Subarachnoid hemorrhage · Vasospasm

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Introduction

The development of pulmonary complications following aneurysmal subarachnoid hemorrhage (SAH) is common and may be associated with worse outcomes [1–7]. Pulmonary edema is a particularly frequent complication, and

can have both "cardiogenic" and "noncardiogenic" [acute lung injury (ALI) or acute respiratory distress syndrome (ARDS)] etiologies [8–13]. The causes of pulmonary edema may vary depending on whether it develops "early" or "late" in the course of disease. During the first few days after aneurysm rupture, bilateral infiltrates are usually attributed to neurogenic pulmonary edema, aspiration pneumonitis, or cardiogenic pulmonary edema complicating neurogenic-stunned myocardium. These etiologies can be difficult to distinguish; even if impaired cardiac function is demonstrated using invasive hemodynamic monitoring or echocardiography, this does not necessarily prove that the pulmonary edema is cardiogenic in origin. Furthermore, both raised hydrostatic pressure (from impaired cardiac function and pulmonary venoconstriction) and increased alveolar–capillary permeability are likely to be involved in the pathogenesis of neurogenic pulmonary edema [9–14]. The subsequent development of pulmonary infiltrates is typically due to other conditions, such as nosocomial pneumonia, iatrogenic fluid overload complicating the management of cerebral vasospasm, or ALI/ARDS caused by extra-pulmonary sepsis. Because of the difference in etiologies, it is possible that early and late pulmonary infiltrates have different natural histories and prognostic implications. Although the incidence of ALI in SAH was recently described [7], the relative proportion of early versus late bilateral infiltrates, as well as their association with eventual outcomes, is largely unknown. This distinction may be important because late infiltrates are potentially more amenable to prevention.

Methods

This was a retrospective cohort study utilizing a database of consecutive patients with aneurysmal SAH admitted to the Neuroscience Intensive Care Unit (ICU) at the University of Virginia between November 2003 and February 2007. The study was approved by the institutional review board. Management of SAH was consistent with published guidelines and has been described in detail elsewhere [15–17]. We excluded patients who had life-sustaining therapies withdrawn within 72 h of admission because of either death by neurologic criteria or the perception of a dismal prognosis. Because of the devastating nature of their neurologic injury, it is unlikely that the clinical course of these patients would have been altered by systemic complications (including pulmonary infiltrates) or subsequent medical care.

All printed chest radiograph reports from patients in the cohort were screened, and cases of bilateral pulmonary infiltrates were identified. Chest radiographs were interpreted by radiologists not involved in the study. Pulmonary infiltrates could be attributable to cardiogenic pulmonary edema, ALI/ARDS, bilateral pneumonia, or other causes of pneumonitis. Infiltrates attributable only to atelectasis or pleural effusions were excluded. All information regarding pulmonary complications was extracted from the patients' medical records by the principle investigator (AK), who was, at the time, blinded to subsequent outcomes. Charts were also reviewed to ascertain the degree of gas exchange impairment and to determine whether the treating team believed the infiltrates to be due to cardiac dysfunction and/or volume overload. Patients were classified as having ARDS if the P_aO_2:FiO_2 ratio was less than 200 and if the infiltrates were deemed not to be due to cardiogenic pulmonary edema [18]. Since some patients with pulmonary infiltrates were not mechanically ventilated and did not have arterial blood gas measurements, determination of ALI (P_aO_2:FiO_2 ratio <300) could not reliably be made. Few patients had pulmonary artery catheters. Echocardiograms, electrocardiograms, and troponin levels were not recorded in the database.

We chose a priori to classify pulmonary infiltrates as "early" if they occurred within 72 h of SAH, and "late" if they occurred thereafter. Although this cutoff is somewhat arbitrary, it allowed us to identify patients with early infiltrates even if they did not have chest radiographs performed within the first 24–48 h. Furthermore, most hospital-acquired causes of pulmonary infiltrates, such as ventilator-associated pneumonia or iatrogenic volume overload, would be unusual within 72 h of admission. Patients who did not present to hospital until more than 72 h after the onset of symptoms were assumed not to have had any preceding pulmonary complication.

Initial neurologic status was classified using the World Federation of Neurological Surgeons (WFNS) scale [1 = Glasgow Coma Scale (GCS) 15 and no motor deficit; 2 = GCS 13–14 and no motor deficit; 3 = GCS 13–14 with motor deficit; 4 = GCS 7–12; 5 = GCS 3–6] [19]. Computed tomography (CT) scans were described according to the Modified Fisher Scale (MFS) [0 = no SAH or intraventricular hemorrhage (IVH); 1 = focal or diffuse thin SAH, no IVH; 2 = focal or diffuse, thin SAH, with IVH; 3 = focal or diffuse, thick SAH, no IVH; 4 = focal or diffuse, thick SAH, with IVH] [20]. Patient outcomes were graded using the Glasgow Outcome Scale (GOS) [21]. In most (88%) of the surviving patients, final assessment was made at follow-up appointments six weeks after discharge; the outcomes of the remaining patients were carried forward from last contact. A "good" outcome was defined as a GOS of 4 (moderate disability) or 5 (good recovery), while a "poor" outcome was defined as a GOS of 1–3 (dead, vegetative state, or severe disability).

To be classified as having clinical vasospasm, a patient needed to meet all three of the following criteria: (1) There

was a change in neurologic status not attributable to another etiology (e.g., seizure, hydrocephalus, infection, or electrolyte disturbance); (2) Vascular imaging (CT, magnetic resonance or digital subtraction angiography) performed after the onset of symptoms was interpreted by a neuroradiologist as demonstrating at least moderate radiographic vasospasm (>33% narrowing); (3) Symptoms were sufficiently severe and persistent for physicians to initiate treatment. Determination of the presence or absence of vasospasm was made by the principle investigator (AK), using neuroradiologist reports. Clinical vasospasm was always treated with additional volume expansion using intravenous albumin ± crystalloid and blood pressure augmentation with norepinephrine or phenylephrine. If there was still no improvement, angiography was performed, with the administration of intra-arterial verapamil ± angioplasty.

Statistical analysis was completed using SAS (Version 9.2; Cary, NC). Between-group comparisons were performed using the Student's *t*-test for continuous variables, and chi-square analysis or Fisher's exact test for categorical variables. In comparing patients with and without pulmonary infiltrates, we adjusted for potentially confounding variables using multiple logistic regression. We chose a priori to adjust for age (by decade), initial neurologic status (using the WFNS scale), amount of blood on the initial CT scan (using the MFS), and the presence of symptomatic vasospasm. These covariates have consistently been identified as key predictors of outcome [22, 23]. Other collected variables included patient sex, history of hypertension or diabetes mellitus, aneurysm location (posterior vs. anterior), aneurysm diameter (in mm), and the method of aneurysm treatment (clip vs. coil). These variables were only incorporated into the multivariable models if they differed significantly between the groups being compared ($P < 0.15$), and if there was a significant association with the outcome of interest in univariate analysis, using 2×2 tables ($P < 0.15$). For all other analyses, a *P*-value less than 0.05 was considered to be statistically significant.

Results

The entire cohort consisted of 272 consecutive patients with radiographically proven aneurysmal SAH. Twenty-seven patients, all of whom had an initial WFNS score of 5, were excluded because of death by neurologic criteria or a transition to palliative care within three days of admission. Of the remaining 245 patients, 67 (27%) developed bilateral pulmonary infiltrates at some point during their hospital stay. The clinical characteristics of the cohort, dichotomized based on whether or not patients developed bilateral pulmonary infiltrates, are summarized in Table 1. Patients with infiltrates were more likely to have presented with a depressed level of consciousness (higher WFNS score; $P < 0.01$), tended to have more blood on the initial CT scan (higher MFS score; $P < 0.01$), more often had a history of preceding hypertension (57% vs. 37%; $P < 0.01$), and were more likely to develop clinical vasospasm during their hospital admission (36% vs. 22%; $P = 0.03$).

The greatest proportion of bilateral pulmonary infiltrates occurred within the first 24–48 h after SAH (Fig. 1). Of the 67 patients with bilateral pulmonary infiltrates, 36 (54%) had only "early" infiltrates and 24 (36%) had only "late" infiltrates. Seven (10%) patients developed early infiltrates, which subsequently resolved, but were later followed by recurrent pulmonary disease. The characteristics of these patients are described in Table 2. Patients with exclusively early disease were significantly more likely to have presented with stupor or coma (WFNS 4 or 5) than patients who developed infiltrates later (64% vs. 29%; $P < 0.01$). A substantial proportion of patients who developed late pulmonary infiltrates (16 out of 31; 52%) were being treated for clinical vasospasm at the time. In contrast, because vasospasm typically occurs beyond 72 h after SAH, none of the patients with exclusively early infiltrates were being treated for vasospasm at the time. Patients with late pulmonary infiltrates were also somewhat more likely to have been diagnosed with nosocomial pneumonia (42% vs. 33%), but this difference did not reach statistical significance.

In univariate analysis (Table 3), patients who developed bilateral pulmonary infiltrates at some point during their hospitalization were more likely to die [31% vs. 9%; odds ratio (OR) 4.6, 95% CI 2.2–9.6; $P < 0.01$] or have a poor outcome (60% vs. 27%; OR 4.0, 95% CI 2.2–7.2; $P < 0.01$). The length of hospital stay was also greater among these patients (19.6 days vs. 15.3 days, $P < 0.01$). The same pattern of findings was observed in both subgroups (early or late), although the differences were more pronounced among those with late infiltrates. Twenty-eight (11%) patients were categorized as meeting criteria for ARDS. In the majority of cases (20/28, 71%), ARDS occurred within 72 h of SAH. ARDS had a univariate association with death (OR 3.9, 95% CI 1.6–9.3; $P < 0.01$), but did not reach statistical significance in predicting the composite of death or poor functional outcome (OR 1.9, 95% CI 0.9–4.3; $P = 0.10$).

Apart from the potential confounders chosen a priori for incorporation into the multivariable models, the only other variable found to be significantly associated with poor neurologic outcome was a preceding history of hypertension (OR 1.7, 95% CI 1.0–2.9; $P = 0.03$). Although aneurysm diameter differed between patients with and without pulmonary infiltrates, it was not significantly

Table 1 Patient characteristics based on whether or not they ever developed bilateral pulmonary infiltrates

Variable	Pulmonary infiltrates[a] (67)	No pulmonary infiltrates (178)	*P*-value
Age (mean, 95% CI)	57.1 (54.0–60.2)	53.8 (51.9–55.8)	0.08
Sex			
Female	50 (76%)	118 (66%)	0.21
Male	17 (25%)	60 (34%)	
WFNS[b]			
1	13 (19%)	90 (51%)	<0.01
2	12 (18%)	49 (28%)	
3	7 (11%)	9 (5%)	
4	26 (39%)	25 (14%)	
5	9 (13%)	5 (3%)	
MFS[c]			
0	2 (3%)	6 (3%)	<0.01
1	2 (3%)	33 (19%)	
2	11 (16%)	39 (22%)	
3	9 (13%)	27 (15%)	
4	43 (64%)	73 (41%)	
Aneurysm location			
Anterior	58 (87%)	147 (83%)	0.45
Posterior	9 (13%)	31 (17%)	
Aneurysm diameter (mm, 95% CI)	6.6 (5.7–7.5)	6.4 (5.8–6.9)	0.63
Aneurysm treatment			
Clip	40 (60%)	110 (62%)	0.33
Coil	27 (40%)	63 (35%)	
Neither	0	5 (3%)	
Hypertension	38 (57%)	66 (37%)	<0.01
Diabetes	9 (13%)	16 (9%)	0.31
Clinical vasospasm	24 (36%)	40 (22%)	0.03

[a] Pulmonary infiltrates could be due to cardiogenic or noncardiogenic pulmonary edema, bilateral pneumonia, or other causes of pneumonitis. Those due only to atelectasis or pleural effusions were excluded

[b] WFNS = World Federation of Neurological Surgeons scale

[c] MFS = Modified Fisher Scale

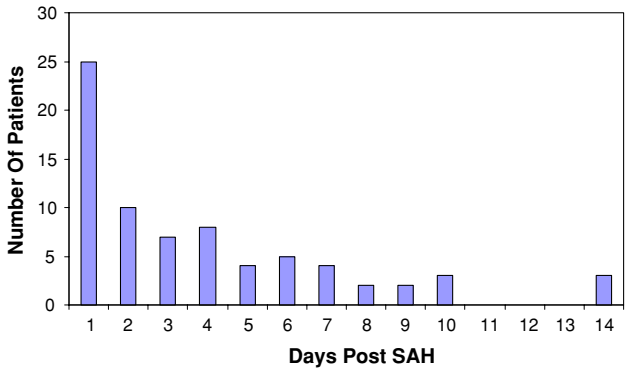

Fig. 1 Number of patients developing bilateral pulmonary infiltrates on each of the first 14 days following aneurysmal SAH (out of 67 total patients)

predictive of poor outcome (mean diameter if good outcome = 6.3 mm, 95% CI 5.5–7.0; mean diameter if poor outcome = 6.5 mm, 95% CI 5.9–7.1; $P = 0.68$), and was therefore not included in the multivariable models. In assessing the association between bilateral pulmonary infiltrates and outcome, we therefore adjusted for age (by decade), WFNS (dichotomized into categories of 1–3 vs. 4–5), MFS (dichotomized into categories of 0–2 vs. 3–4), clinical vasospasm and a history of hypertension (Table 4). Overall, the development of bilateral pulmonary infiltrates remained an independent predictor of both death (OR 2.5, 95% CI 1.1–5.8; $P = 0.04$) and poor outcome (OR 2.5, 95% CI 1.2–5.2; $P = 0.02$). However, this was true only for the subgroup of patients who developed late pulmonary infiltrates (OR for death 3.5, 95% CI 1.3–9.4; $P = 0.01$; OR for poor outcome 5.0, 95% CI 1.9–13.6; $P < 0.01$), but not for those with early infiltrates (OR for death 1.4, 95% CI 0.5–3.5; $P = 0.52$; OR for poor outcome 1.2, 95% CI 0.5–3.0; $P = 0.66$). The development of ARDS was not significantly predictive of adverse outcomes in multivariable analysis (OR for death 2.0, 95% CI 0.7–5.6; $P = 0.20$; OR for poor outcome 1.6, 95% CI 0.5–4.5; $P = 0.42$).

Discussion

Pulmonary complications are common following aneurysmal SAH. In fact, gas exchange is frequently deranged

Table 2 Patient characteristics based on whether they developed bilateral pulmonary infiltrates "early" (≤72 h) or "late" (>72 h) following aneurysmal subarachnoid hemorrhage

Variable	Early infiltrates[a] (36)	Late infiltrates (24)	Early and late infiltrates (7)	*P*-value (early vs. late)
Age (mean, 95% CI)	57.4 (52.6–62.2)	57.7 (52.6–62.8)	53.3 (47.6–59.0)	0.93
Sex				
Female	26 (72%)	19 (79%)	5 (71%)	0.54
Male	10 (28%)	5 (21%)	2 (29%)	
WFNS[b]				
1–3	13 (36%)	17 (71%)	2 (29%)	<0.01
4–5	23 (64%)	7 (29%)	5 (71%)	
MFS[c]				
0–2	10 (28%)	5 (21%)	0	0.54
3–4	26 (72%)	19 (79%)	7 (100%)	
Aneurysm location				
Anterior	31 (86%)	21 (88%)	6 (86%)	0.88
Posterior	5 (14%)	3 (13%)	1 (14%)	
Aneurysm diameter (mm, 95% CI)	5.5 (4.7–6.2)	8.1 (6.1–10.1)	7.5 (2.9–12.1)	0.02
Aneurysm treatment				
Clip	19 (53%)	17 (71%)	4 (57%)	0.16
Coil	17 (47%)	7 (29%)	3 (43%)	
Hypertension	21 (58%)	12 (50%)	5 (71%)	0.53
Diabetes	6 (17%)	3 (13%)	0	0.66
Clinical vasospasm				
Overall	10 (28%)	11 (46%)	3 (43%)	0.15
At time of infiltrates	0	9 (38%)	7 (100%)	<0.01
Nosocomial pneumonia				
Overall	12 (33%)	10 (42%)	5 (71%)	0.51
Diagnosis coinciding with onset of infiltrates	4 (17%)	2 (6%)	1 (14%)	0.21

[a] Pulmonary infiltrates could be due to cardiogenic or noncardiogenic pulmonary edema, bilateral pneumonia, or other causes of pneumonitis. Those due only to atelectasis or pleural effusions were excluded

[b] WFNS = World Federation of Neurological Surgeons score

[c] MFS = Modified Fisher Scale

Table 3 Univariate associations between pulmonary infiltrates and outcomes

Outcome	Pulmonary infiltrates[a]								
	Overall			Early (≤72 h)			Late (>72 h)		
	Yes ($n = 67$)	No ($n = 178$)	*P*-value	Yes ($n = 42$)	No ($n = 203$)	*P*-value	Yes ($n = 31$)	No ($n = 214$)	*P*-value
Death	21 (31%)	16 (9%)	<0.01	13 (31%)	24 (12%)	<0.01	11 (36%)	26 (12%)	<0.01
Glasgow Outcome Scale 1–3[b]	40 (60%)	48 (27%)	<0.01	22 (52%)	66 (33%)	0.01	23 (74%)	65 (30%)	<0.01
Length of stay (mean no. days)	19.6 (17.1–22.2)	15.3 (14.0–16.6)	<0.01	19.4 (15.8–23.0)	15.9 (14.7–17.1)	0.07	22.4 (18.1–26.7)	15.6 (14.5–16.8)	<0.01

[a] Pulmonary infiltrates could be due to cardiogenic or noncardiogenic pulmonary edema, bilateral pneumonia, or other causes of pneumonitis. Those due only to atelectasis or pleural effusions were excluded

[b] Glasgow Outcome Scale: 1 = dead; 2 = vegetative state; 3 = severe disability

even when there are minimal or no radiographic abnormalities, with an increased alveolar-arterial (A-a) oxygen gradient documented in as many as 80% of cases [1, 3]. Our findings that more than a quarter of patients develop bilateral pulmonary infiltrates is consistent with the literature, where either cardiogenic or noncardiogenic

Table 4 Multivariable associations between pulmonary infiltrates and outcomes[a]

Outcome	Pulmonary infiltrates[b]					
	Overall		Early (≤72 h)		Late (>72 h)	
	Odds Ratio (95% CI)	*P*-value	Odds Ratio (95% CI)	*P*-value	Odds Ratio (95% CI)	*P*-value
Death	2.5 (1.1–5.8)	0.04	1.4 (0.5–3.5)	0.52	3.5 (1.3–9.4)	0.01
Glasgow Outcome Scale 1–3[c]	2.5 (1.2–5.2)	0.02	1.2 (0.5–3.0)	0.66	5.0 (1.9–13.6)	<0.01

[a] Variables included in multivariable models: age, WFNS 1–3 vs. 4–5, MFS 0–2 vs. 3–4, clinical vasospasm, history of hypertension

[b] Pulmonary infiltrates could be due to cardiogenic or noncardiogenic pulmonary edema, bilateral pneumonia, or other causes of pneumonitis. Those due only to atelectasis or pleural effusions were excluded

[c] Glasgow Outcome Scale: 1 = dead; 2 = vegetative state; 3 = severe disability

pulmonary edema has been reported with a prevalence of 14–29% [1–5, 7]. The widely accepted American–European consensus definition for ARDS has not been previously applied specifically to patients with SAH. Using these criteria, we found the prevalence of ARDS in our cohort to be 11%. Khan et al. found the incidence of ALI among patients with aneurysmal SAH to be 27%, but did not report the proportion of patients with ARDS [7].

The existing literature varies regarding the prognostic importance of pulmonary infiltrates in SAH. Some studies have suggested that pulmonary complications independently predict outcomes [3, 4, 6, 7], while others have not [2, 5]. By differentiating between early and late infiltrates, our findings elaborate on this relationship. Early pulmonary infiltrates were considerably more common among patients with high grade SAH (WFNS 4–5) and large amounts blood on their initial CT scan (MFS 3–4). As a result, there was (as expected) also a strong univariate association with subsequent outcomes. However, early infiltrates were not predictive of adverse outcome in our *multivariable* analysis, suggesting that the degree of neurologic injury is a much more important determinant of outcome than concomitant early pulmonary complications. Even the early development of ARDS (with a relatively severe degree of hypoxemia) was not an independent predictor of adverse outcome.

In contrast, late pulmonary infiltrates were strongly and independently associated with death, poor functional outcome, and longer length of stay. These findings indicate that early and late infiltrates not only have varying etiologies, but also a different natural history and prognosis. The presence of either nosocomial pneumonia or clinical vasospasm was relatively common among patients with late pulmonary infiltrates (Table 2). Clearly, the aggressive use of volume expansion as part of "triple H therapy" may have contributed to pulmonary edema formation. However, vasospasm could also predispose to ALI/ARDS by other mechanisms; firstly, aggressive use of vasopressors to target supranormal blood pressure has been linked with the development of ALI/ARDS in patients with traumatic brain injury [24], and could have a similar effect when used as part of "triple H therapy"; secondly, vasospasm is associated with cerebral and systemic inflammation, which could predispose patients to the development of ALI/ARDS [25].

Our observation that early pulmonary infiltrates are not predictive of adverse outcome differs somewhat from the findings of Claassen et al., who reported that that an A-a gradient of more than 125 within the first 24 h is associated with later death or severe disability [6]. It remains conceivable that the degree of gas exchange impairment, rather than only the presence of radiographic infiltrates per se, may be related to eventual outcome. Unfortunately, because we did not obtain arterial blood gases on all patients during the time that they had pulmonary infiltrates (particularly those who were not mechanically ventilated), we cannot explore this possibility further.

Although our retrospective findings should be regarded primarily as hypothesis-generating, they suggest that increased vigilance in the avoidance of late pulmonary complications (e.g., more careful fluid management in patients with symptomatic vasospasm or use of evidence-based approaches to the prevention of ventilator-associated pneumonia) could lead to improved overall outcomes among patients with SAH. Neurocritical care frequently involves balancing what is best for the brain with what is most appropriate for other organ systems. The optimal approach to ensuring sufficient cerebral perfusion in the face of cerebral vasospasm specifically requires further study. Although hypovolemia is clearly deleterious [26], over-aggressive fluid administration has little effect on cerebral blood flow, and may compromise brain tissue oxygenation [27].

There are several observations from our data that argue in favor of neurogenic pulmonary edema as perhaps the predominant mechanism responsible for bilateral infiltrates in this patient population. Firstly, we found a strong association between higher grade SAH (WFNS 4–5 and MFS 3–4) and the development of pulmonary infiltrates. The pathogenesis of neurogenic pulmonary edema is

thought to begin with excessive stimulation of the sympathetic nervous system [14]. One would therefore expect this effect to be more pronounced among patients with more severe neurologic injury. Accordingly, one study of patients with fatal SAH found more than 70% to have pulmonary edema at autopsy [28]. Secondly, we found that in the majority of cases (64%), pulmonary infiltrates occurred early in the course of disease, most often within the first 24 h. In keeping with this observation, most cases of neurogenic pulmonary edema are thought to develop within hours of neurologic injury. Finally, our finding that early pulmonary infiltrates were not independently predictive of adverse outcomes is consistent with a condition that is known to have a different natural history than other causes of ALI/ARDS, typically with a considerably shorter course [14].

Our study has several limitations. Few patients had direct measurement of their cardiac output (e.g., with a pulmonary artery catheter or alternative method), and the results of cardiac investigations (troponin levels, echocardiogram, and electrocardiogram reports) were not recorded as part of our database; thus, the differentiation between cardiogenic and noncardiogenic pulmonary infiltrates was based largely only on physicians' clinical impression. Nevertheless, even with invasive hemodynamic monitoring, determining the cause of pulmonary infiltrates with certainty is usually not straightforward [8–11, 13]. Several outcomes were determined retrospectively, and were therefore more vulnerable to misclassification and bias, despite efforts to ensure blinding during the extraction of information from the medical records. Final patient outcomes were ascertained after six weeks, even though patients with SAH sometimes improve beyond this time [29]. Outcomes of some surviving patients (12%), particularly those with severe disability who were unable to return to clinic for follow-up, were carried forward from last contact at the time of hospital discharge. However, this is unlikely to have influenced our results, since it is relatively unusual for patients with "poor outcome" to transition to "good outcome" (and vice versa) in such a short period of time.

Conclusion

Bilateral pulmonary infiltrates developed in 27% of our patients with aneurysmal SAH. Although we could not specifically determine the prevalence of ALI, 11% of patients met criteria for ARDS. Most cases occur soon after aneurysm rupture, and are particularly likely among patients with a more severely impaired level of consciousness. However, only infiltrates occurring beyond three days are independently associated with poor outcome. Future studies should take this difference in natural history and prognosis into account. Increased emphasis on the prevention of late pulmonary complications has the potential to significantly improve outcomes in patients with SAH.

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